Extending X-ray Crystallography to Non-Crystalline Specimens by the Oversampling Method

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Sampling the diffraction pattern of a finite specimen at a spacing finer than the Nyquist frequency (*i.e.* the inverse of the size of the specimen) corresponds to surrounding the electron density of the specimen with a region of mathematically zero charge-density. The finer the sampling frequency, the larger the zero-density region. If the zero-density region is larger than the electron density region, the phase information is in principle imbedded inside the diffraction pattern and can be directly retrieved by using a modification of Fienup's iterative algorithm. In this talk, I will review a theory which was proposed by some of us to explain why the phase information is uniquely imbedded inside an oversampled diffraction pattern, and present some experimental results which support the theory. Two important potential applications will be illustrated: (i) imaging 3D mesoporous nanoscale materials and inorganic nanostructures at 5 – 10 nm resolution and (ii) imaging single biomolecules at high resolution by utilizing X-ray free electron laser (X-FEL) exposures. I will report the progress we have made in recording high-resolution oversampled diffraction patterns from 2D and 3D test specimens and mesoporous materials (*i.e*. MCM-48 particles) at APS and SSRL. Finally, I will present our computer modeling results showing that a simulated molecular diffraction pattern at 2.5 Å resolution accumulated from multiple copies of single rubisco biomolecules each generated by a femtosecond X-FEL pulse can be successfully phased and transformed into an accurate electron density map comparable to that obtained by more conventional methods. The combination of the oversampling method with the extreme brightness and ultra-short time structure of the X-ray free electron lasers could hence provide a major new opportunity for the high resolution three-dimensional structure determination of single biomolecules.

References

1. Bates, R. H. T. Fourier phase problems are uniquely solvable in more than one dimension. I: underlying theory. *Optik* **61**, 247-262 (1982).
2. Fienup, J. R. Phase retrieval algorithm: a comparison. *Appl. Opt.* **21**, 2758-2769 (1982).

3. Sayre, D., Chapman, H. N. & Miao, J. On the extendibility of X-ray crystallography to noncrystals. *Acta Crystallogr*. A **54**, 233-239 (1998).
4. Miao, J., Sayre, D. & Chapman, H. N. Phase retrieval from the magnitude of the Fourier transforms of non-periodic objects. *J. Opt. Soc. Am*. A **15**, 1662-1669 (1998).
5. Miao, J., Charalambous, P., Kirz, J. & Sayre, D. Extending the methodology of X-ray crystallography to allow imaging of micrometre-sized non-crystalline specimens. *Nature* **400**, 342-344 (1999).
6. Miao, J., Kirz, J. & Sayre, D. The oversampling phasing method. *Acta Crystallogr*. D **56**, 1312-1315 (2000).
7. Miao, J. & Sayre, D. On possible extensions of X-ray crystallography through diffraction pattern oversampling. *Acta Crystallogr*. A **56**, 596-605 (2000).
8. Sayre, D., Miao, J., Kirz, & Charalambous, P. An extension of the methodology of X-ray crystallography allowing imaging of micron-size non-crystalline specimens. in *Proceedings of 2000 Erice conference on Methods in Macromolecular Crystallography* (D. Turk, ed.) (in press).
9. Miao, J, Hodgson, K. O. & Sayre, D. A New Approach to 3D Structures of Biomolecules Utilizing Single Molecule Diffraction Images. submitted (2001).